Europäisches Patentamt

European Patent Office

Office européen des brevets



EP 0 860 433 A1

(12)

# **EUROPEAN PATENT APPLICATION**

published in accordance with Art. 158(3) EPC

- (43) Date of publication: 26.08.1998 Bulletin 1998/35
- (21) Application number: 96935541.1
- (22) Date of filing: 05.11.1996

- (51) Int. Cl.<sup>6</sup>: **C07D 215/20**, C07D 215/22, C07D 215/36, C07D 239/74, C07D 239/88, C07D 239/93, C07D 401/12, C07D 405/12, C07D 409/12, C07D 491/056, A61K 31/47
- (86) International application number: PCT/JP96/03229

(11)

(87) International publication number: WO 97/17329 (15.05.1997 Gazette 1997/21)

- (84) Designated Contracting States: CH DE FR GB LI
- (30) Priority: 07.11.1995 JP 313555/95 23.02.1996 JP 62121/96
- (71) Applicant: KIRIN BEER KABUSHIKI KAISHA Chuo-Ku, Tokyo 104 (JP)
- (72) Inventors:
  - KUBO, Kazuo, Iyaku Tansaku Kenkyusho Takasaki-shi, Gunma 370-12 (JP)
  - OHYAMA, Shinichi, Iyaku Tansaku Kenkyusho Takasaki-shi, Gunma 370-12 (JP)
  - SHIMIZU, Toshiyuki, Iyaku Tansaku Kenkyusho Takasaki-shi, Gunma 370-12 (JP)

- NISHITOBA, Tsuyoshi, lyaku Tansaku Kenkyusho Takasaki-shi, Gunma 370-12 (JP)
- KATO, Shinichiro, Iyaku Tansaku Kenkyusho Takasaki-shi, Gunma 370-12 (JP)
- MUROOKA, Hideko, Iyaku Tansaku Kenkyusho Takasaki-shi, Gunma 370-12 (JP)
- KOBAYASHI, Yoshiko, Iyaku Tansaku Kenkyusho Takasaki-shi, Gunma 370-12 (JP)
- (74) Representative:
  Kolb, Helga, Dr. Dipl.-Chem. et al Hoffmann Eitle, Patent- und Rechtsanwälte, Arabellastrasse 4 81925 München (DE)
- (54) QUINOLINE DERIVATIVES AND QUINAZOLINE DERIVATIVES INHIBITING
  AUTOPHOSPHORYLATION OF GROWTH FACTOR RECEPTOR ORIGINATING IN PLATELET
  AND PHARMACEUTICAL COMPOSITIONS CONTAINING THE SAME
- (57) The present invention relates to novel quinoline derivatives and quinazoline derivatives represented by the following formula (I):

EP 0 860 433 A1

The results shown above revealed that the compound number 43 suppressed the incidence of collagen-induced arthritis.

### Possible Industrial Use

Since the compounds of the present invention have inhibitory activity on abnormal cell growth, more specifically PDGF receptor autophosphorylation inhibitory activity, they are useful for treating numerous diseases such as leukemia, cancers, psoriasis, glomerulonephritis, organofibrosis, atherosclerosis, restenosis after percutaneous coronary angioplasty or bypass surgery and articular rheumatism. Therefore, the compounds can benefit greatly in treating humans and other animals which need these treatments.

### Claims

15

25

30

35

40

45

50

55

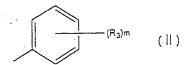
1. Quinoline derivatives and quinazoline derivatives represented by the following formula (I):

$$R_1O$$
 $R_2O$ 
 $N$ 
 $N$ 
 $N$ 
 $N$ 

{wherein  $R_1$  and  $R_2$  are each independently H,  $C_1$ - $C_5$ -alkyl, or  $R_1$  and  $R_2$  together form  $C_1$ - $C_3$ -alkylene, and W is CH or N.

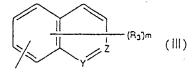
# (1) when W is CH,

(a) X is O or S, and Q is a phenyl group represented by formula (II):



[wherein m is 1, 2 or 3,  $R_3$  is each independently CN, OH, halogen,  $C_1$ - $C_5$ -alkyl,  $C_1$ - $C_4$ -alkoxy or  $C_2$ - $C_4$ -acyl],

a group represented by formula (III):



[wherein m is as defined as described above,  $R_3$ ' is each independently OH,  $C_1$ - $C_5$ -alkyl,  $C_1$ - $C_4$ -alkoxy, and Y and Z are both or each independently N or CH], or a group represented by formula (IV):

[wherein m and  $R_3$ ' are as defined as described above, and  $R_4$  is H,  $C_1$ - $C_5$ -alkyl or  $C_2$ - $C_4$ -acyl], and (b) X is O, S or CH<sub>2</sub>, and Q is a group represented by formula (V):

[wherein j and k are each independently 0 or 1,  $R_5$  is each independently H or  $C_1$ - $C_4$ -alkyl, A is  $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_5$ -alkenyl, cyclic ( $C_3$ - $C_{10}$ ) alkyl,  $C_1$ - $C_4$ -alkoxycarbonyl, phenyl, naphthyl, furyl, thienyl, benzoyl, substituted benzoyl,  $C_2$ - $C_4$ -acyl, or 5- or 6-membered monocyclic or 9- or 10-membered bicyclic heteroaryl group having 1 or 2 nitrogen atoms and optionally having another hetero atom selected from the group consisting of nitrogen, oxygen and sulfur atoms, these alkyl group, aryl group and heteroaryl group represented by A may have 1 to 5 substituents selected from the group consisting of CN,  $NO_2$ , OH,  $NH_2$ , halogen,  $C_1$ - $C_5$ -alkyl, cyclic ( $C_3$ - $C_{10}$ ) alkyl,  $C_1$ - $C_4$ -alkoxy,  $C_1$ - $C_4$ -alkoxycarbonyl,  $C_1$ - $C_5$ -acyl,  $C_1$ - $C_5$ -acyl,  $C_1$ - $C_5$ -alkyl)amido,  $C_1$ - $C_3$ -alkyl)amido,  $C_1$ - $C_4$ -alkyl)amido,  $C_1$ - $C_1$ -alkyl)amido,  $C_1$ - $C_2$ -alkylamido,  $C_1$ - $C_2$ -alkylamido,  $C_1$ - $C_2$ -alkylamido,  $C_1$ - $C_2$ -alkylamido,  $C_1$ - $C_2$ -

(2) when W is N, X is O, S or CH2, and Q is represented by formula (V):

10

15

20

25

30

35

40

45

55

$$\begin{array}{c|c}
R_5 & R_5 \\
N) j & N \\
N \\
M
\end{array}$$

$$\begin{array}{c}
R_5 & R_5 \\
N \\
N \\
M
\end{array}$$

$$\begin{array}{c}
A \\
(V)
\end{array}$$

[wherein j, K, R<sub>5</sub>, A and B are defined as described above]] and pharmaceutically acceptable salts thereof.

- Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 1, characterized in that in tormula (I), W is CH, X is O or S, and Q is formula (III), formula (III) or formula (IV).
- Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 1, characterized in that in formula (I), W is CH, X is O, and Q is formula (II), formula (III) or formula (IV).
- Quinoline derivatives and quinazoline derivatives and pharmaceutically acceptable salts thereof according to Claim
  1, characterized in that in formula (I), X is O, S or CH<sub>2</sub>, and Q is formula (V).

- Quinoline derivatives and quinazoline derivatives and pharmaceutically acceptable salts thereof according to Claim

   characterized in that in formula (I), R<sub>1</sub> and R<sub>2</sub> are each independently C<sub>1</sub>-C<sub>5</sub>-alkyl and Q is formula (V), j and k are 0, B is Q, S, NOR<sub>5</sub> (wherein R<sub>5</sub> is C<sub>1</sub>-C<sub>5</sub>-alkyl)].
- Quinoline derivatives and quinazoline derivatives and pharmaceutically acceptable salts thereof according to Claim

   characterized in that in formula (I), R<sub>1</sub> and R<sub>2</sub> are each independently C<sub>1</sub>-C<sub>5</sub>-alkyl and Q is formula (V), both j and k are 1, R<sub>5</sub> is each independently hydrogen or methyl, B is O, S, NH, NCN, NR<sub>6</sub> or NOR<sub>6</sub> (wherein R<sub>6</sub> is C<sub>1</sub>-C<sub>5</sub>-alkyl)].
- 15 8. Quinoline derivatives and quinazoline derivatives of formula (VI)

25

30

35

45

55

[wherein W is CH or N, R<sub>1</sub> and R<sub>2</sub> are each independently C<sub>1</sub>-C<sub>5</sub>-alkyl, A is methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, pentyl, isopentyl, cyclopentyl, cyclopexyl, cyclopetyl, phenyl, naphthyl, furyl, thienyl, pyridyl or pyrimidinyl, and these alkyl group, aryl group or heteroaryl group represented by A may have 1-5 substituents selected from the group consisting of fluoro, chloro, bromo, iodo, cyano, hydroxy, nitro, amino, methylamino, dimethylamino, dipropylamino, dibutylamino, trifluoromethyl, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, methoxy, ethoxy, propoxy, isopropoxy, morpholino, pyrrolidino, piperidino and butoxy] and pharmaceutically acceptable salts thereof.

9. Quinoline derivatives and quinazoline derivatives formula (VII)

$$\begin{array}{c|c} R_5 & R_5 \\ N & N \\ N & N \\ N & N \end{array}$$

$$R_1 O \qquad W$$

$$R_2 O \qquad N \qquad (VII)$$

[wherein W is CH or N, j is 0 and k is 1 or j is 1 and k is 0,  $R_1$  and  $R_2$  are each independently  $C_1$ - $C_5$ -alkyl,  $R_5$  is hydrogen or methyl, A is methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, pentyl, isopentyl, cyclopentyl, cyclohetyl, phenyl, naphthyl, furyl, thienyl, pyridyl or pyrimidinyl, and these alkyl group, aryl group or heteroaryl group represented by A may have 1-5 substituents selected from the group consisting of fluoro, chloro, bromo, iodo, cyano, hydroxy, nitro, amino, methylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, trifluoromethyl, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, methoxy, ethoxy, propoxy, isopropoxy and butoxy] and pharmaceutically acceptable salts thereof.

## 10. Quinoline derivatives and quinazoline derivatives of formula (VIII)

[wherein W is CH or N, R<sub>1</sub> and R<sub>2</sub> are each independently C<sub>1</sub>-C<sub>5</sub>-alkyl, R<sub>5</sub> is each independently hydrogen or methyl, A is C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-alkenyl, cyclopentyl, cyclohexyl, cycloheptyl, C<sub>1</sub>-C<sub>4</sub>-alkoxycarboryl, phenyl, naphthyl, furyl, thienyl, benzoyl, acetyl, pyridyl, pyrimidinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl or morpholino, these alkyl group, aryl group or heteroaryl group perpesented by A may have 1-5 substituents selected from the group consisting of halogen, cyano, CO<sub>2</sub>H, CONH<sub>2</sub>, hydroxy, nitro, amino, C<sub>1</sub>-C<sub>4</sub>-alkylamino, di-(C<sub>1</sub>-C<sub>4</sub>-alkyl)amino, C<sub>1</sub>-C<sub>5</sub>-acyloxy, C<sub>1</sub>-C<sub>5</sub>-acyl, C<sub>1</sub>-C<sub>4</sub>-alkylthio, trifluoromethyl, C<sub>1</sub>-C<sub>5</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-alkoxyl, C<sub>1</sub>-C<sub>4</sub>-alkylylamido, N-C<sub>1</sub>-C<sub>4</sub>-alkyl)amido, N-C<sub>1</sub>-C<sub>4</sub>-alkylamido, phenoxy, substituted phenyl, benzoyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinolyl and quinazolinyl, and B is O, S, NH, NCN, NR<sub>6</sub> or NOR<sub>6</sub> (in which R<sub>6</sub> is methyl)] and pharmaceutically acceptable salts thereof.

### 11. Quinoline derivatives and quinazoline derivatives of formula (IX)

$$\begin{array}{c|c}
R_1O & W \\
R_2O & N
\end{array}$$
(IX)

[wherein W is CH or N,  $R_1$  and  $R_2$  are each independently  $C_1$ - $C_5$ -alkyl,  $R_5$  is each independently hydrogen or methyl, A is  $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_4$ -alkenyl, cyclopentyl, cyclohexyl, cyclohetyl,  $C_1$ - $C_4$ -alkoxycarbonyl, phenyl, naphthyl, furyl, thienyl, benzoyl, acetyl, pyridyl, pyrimidinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl or morpholino, and these alkyl group, aryl group or heteroaryl group represented by A may have 1-5 substituents selected from the group consisting of halogen, cyano,  $CO_2H$ ,  $CONH_2$ , hydroxy, nitro, amino,  $C_1$ - $C_4$ -alkylamino,  $C_1$ - $C_5$ -acyloxy,  $C_1$ - $C_5$ -acyl,  $C_1$ - $C_4$ -alkylhio, trifluoromethyl,  $C_1$ - $C_5$ -alkyl,  $C_1$ - $C_4$ -alkoxyl,  $C_1$ - $C_4$ -alkyl)amido,  $C_2$ - $C_4$ -alkyl)amido,  $C_2$ - $C_4$ -alkyl)amido,  $C_2$ - $C_4$ -alkyl)amido,  $C_2$ - $C_4$ -alkyl)amido, ethylenedioxy, phenyl, phenoxy, substituted phenyl, benzoyl, pyridyl, pyrazinyl, pyrimidinyl pyridazinyl, quinolyl and quinazolinyl] and pharmaceutically acceptable salts thereof.

- Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 8, characterized in that in formula (VI), W is CH.
- Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 9, characterized in that in formula (VII), W is CH.
- Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 10, characterized in that in formula (VIII), W is CH.
- Quinoline derivatives and pharmaceutically acceptable salts thereof according to Claim 11, characterized in that in formula (IX), W is CH.
- 40 16. Quinoline derivatives and quinazoline derivatives of formula (X)

5

10

15

20

25

30

35

45

50

55

$$\begin{array}{c} R_{1}S \\ N \\ N \end{array} \qquad (X)$$

$$R_{2}O \qquad N \qquad (X)$$

(wherein W is CH or N,  $R_1$  and  $R_2$  are each independently  $C_1$ - $C_5$ -alkyl,  $R_5$  is each independently hydrogen or methyl, A is  $C_1$ - $C_5$ -alkyl, cyclopentyl, cyclohexyl, cycloheptyl, allyl,  $C_1$ - $C_4$ -alkoxycarbonyl, phenyl, naphthyl or ben-

zoyl, and these alkyl group or aryl group represented by A may have 1-5 substituents selected from the group consisting of OH, CO<sub>2</sub>H, fluoro, chloro, bromo, iodo, nitro, amino, di-(C<sub>1</sub>-C<sub>4</sub>-alkyl)amino, ethylenedioxy, acetoxy, methylthio, C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl, trifluoromethyl, C<sub>1</sub>-C<sub>4</sub>-alkyl, pyridyl and phenyl] and pharmaceutically acceptable salts thereof.

Quinoline derivatives and quinazoline derivatives of formula (XI)

5

10

15

20

25

30

35

50

55

[wherein W is CH or N,  $R_1$  and  $R_2$  are each independently  $C_1$ - $C_5$ -alkyl,  $R_5$  is each independently hydrogen or methyl, A is  $C_1$ - $C_5$ -alkyl, cyclopentyl, cycloheptyl, cycloheptyl, allyl,  $C_1$ - $C_4$ -alkoxycarbonyl, phenyl, naphthyl or benzoyl, and these alkyl group or aryl group represented by A may have 1-5 substituents selected from the group consisting of OH,  $CO_2$ H, fluoro, chloro, bromo, iodo, nitro, amino, di- $(C_1$ - $C_4$ -alkyl)amino, ethylenedioxy, acetoxy, methylthio,  $C_1$ - $C_4$ -alkoxycarbonyl, trifluoromethyl,  $C_1$ - $C_4$ -alkyl,  $C_1$ - $C_4$ -alkoxy, pyridyl and phenyl], and pharmaceutically acceptable salts thereof.

- 18. Quinoline derivatives and quinazoline derivatives according to Claim 1, characterized in that in formula (I), W is CH, X is O, both R<sub>1</sub> and R<sub>2</sub> are methyl, Q is formula (V) [ in formula (V), j and k are each independently 0 or 1, R<sub>5</sub> is hydrogen, A is C<sub>1</sub>-C<sub>5</sub>-alkyl, cyclopentyl, cyclohexyl, cycloheptyl, allyl, C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl, phenyl, naphthyl or benzoyl, these alkyl group, aryl group or heteroaryl group represented by A may have 1-5 substituents selected from the group consisting of OH, CO<sub>2</sub>H, fluoro, chloro, bromo, iodo, nitro, amino, di-(C<sub>1</sub>-C<sub>4</sub>-alkyl)amino, ethylenedioxy, acetoxy, methylthio, C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl, trifluoromethyl, C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy, pyridyl and phenyl, and B is O, S, NH, NCN, NR<sub>6</sub> or NOR<sub>6</sub> (in which R<sub>6</sub> is methyl)] and pharmaceutically acceptable salts thereof.
- 19. Compounds according to Claim 16, characterized in that in formula (I), W is CH, both R<sub>1</sub> and R<sub>2</sub> are methyl, and each R<sub>5</sub> is hydrogen, and pharmaceutically acceptable salts thereof.
- Compounds of formula (I) according to Claim 1 selected from 6,7-dimethoxy-4-(2-methoxyphenoxy)quinoline, 6,7-dimethoxy-4-(3-methoxyphenoxy)quinoline, 6,7-dimethoxy-4-(3-methoxyquinoline, 4-(3-fluorophenoxy)-6,7-dimethoxyquinoline, 4-(3-fluorophenoxy)-6,7-dimethoxyquinoline, 6,7-dimethoxyquinoline, 6,7-dimethoxyphenoxy)-6,7-dimethoxyquinoline, 6,7-dimethoxy-4-(3-methoxy-4-(1-naphthyloxy)quinoline, 6,7-dimethoxy-4-(6-methoxy-2-naphthyloxy)quinoline, 6,7-dimethoxy-4-(6-methoxy-2-naphthyloxy)quinoline, 6,7-dimethoxy-4-(6-methoxy-2-naphthyloxy)quinoline, 6,7-dimethoxy-4-(6-quinolyloxy)quinoline, 4-(4-indolyloxy)-6,7-dimethoxyquinoline, 6,7-dimethoxy-4-(6-quinolyloxy)quinoline, 4-(4-indolyloxy)-6,7-dimethoxyquinoline, 6,7-dimethoxy-4-(3-methoxyphenytthio)quinoline, and 6,7-dimethoxy-4-(4-methoxyphenytthio)quinoline, and pharmaceutically acceptable salts thereof.
  - 21. Compounds of formula (I) according to Claim 1 selected from (4-n-butylphenyl){4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}methanone, (4-t-butylphenyl)[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]methanone, (4-t-butylphenyl)[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]methanone, (4-t-butylphenyl)[4-[(6,7-dimethoxy-4-quinolyl)]methanone, (4-t-butylphenyl)[4-[(6,7-dimethoxy-4-quinolyl)]methanone, N-[4-[(6,7-dimethoxy-4-quinolyl)]methanone, N-[4-[(6,7-dimethoxy-4-quinol

### EP 0 860 433 A1

5

10

15

20

35

N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-(4-bromophenyl)carboxamide. phenyl)carboxamide, dimethoxy-4-quinolyl)oxy]phenyl]cyclopontanecarboxamide, N-(4-n-butylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, N-(4-t-butylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, N-(2-trifluoromethylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxylphenyl}urea. N-(3-trifluoromethylphenyl)-N'-{4-[(6,7-dimethoxy-4quinolyl)oxy]phenyl]urea, N-(4-trifluoromethylphenyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxy]phenyl}urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxy]phenyl}urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxy]phenyl}urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxy]phenyl}urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxy]phenyl}urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxyphenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxyphenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxyphenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxyphenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxyphenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxyphenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxyphenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxyphenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxyphenyl)oxyphenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6, quinoiyi)oxy]phenyl]urea, N-(4-methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, N-(2-fluorophenyl)-N'-{4-[(6.7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3-fluorophenyl)-N'-{4-f(6,7-dimethoxy-4-quinoiyi)oxy]phenyi]urea, N-(4-fluorophenyi)-N'-{4-[(6,7-dimethoxy-4-quinolyi)oxy]phenyi]urea, N-(4-acetylphenyi)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-n-propylurea, N-nbutyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl)phenylurea, N-(2-fluorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]urea, N-(2-methoxyphenyl)-N'-(4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]urea, N-(3-methoxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]urea, N-(4-methoxyphenyl)-N'-[4-[(6,7-dimethoxy-4quinazolinyl)oxy]phenyl}urea, N-n-butyl-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea, {4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea, {4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylurea, {4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylurea, {4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylurea, {4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylurea, {4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylurea, {4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylurea, {4-[(6,7-dimethoxy-4-quinazolinylurea, {4-[(6,7-dimethoxy-4-quinazolinylurea, {4-[(6,7-dimethoxy-4-quinazolinylurea, {4-[(6,7-dimethoxy-4-quinazolinylurea, {4-[(6,7-dimethox 4-quinolyl)oxy]phenyl][4-morpholinophenyl]methanone, [4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl][4-pyrrolidinophenyl]methanone, {4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl][4-piperidinophenyl]methanone, N-(2,4-dichlo-N-(3,4-dichlorophenyl)-N'-(4-[(6,7-dimethoxy-4rophenyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, quinolyl)oxy]phenyl]urea, N-(3,5-dichlorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, N-(4-chloro-2methylphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea, N-(3-amino-4-chlorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-pyridylmethyl)urea, N-(3,4-difluorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, N-(2,4,5-trifiuorophenyl)-N'-{4-[(6,7-dimethoxy-4quinolyl)oxy]phenyl}urea, N-(3-chiorophenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea and N-(4-hydroxyphenyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea, and pharmaceutically acceptable salts thereof.

- 22. A pharmaceutical composition which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and pharmaceutically acceptable safts thereof according to any one of Claims 1-21 having platelet-derived growth factor receptor autophosphorylation inhibitory activity.
- 23. A pharmaceutical composition for use in treating tumors, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.
  - 24. A pharmaceutical composition for use in treating psoriasis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.
  - 25. A pharmaceutical composition for use in treating atherosclerosis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.
  - 26. A pharmaceutical composition for use in treating restenosis after percutaneous coronary angioplasty or bypass surgery, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.
- 45 27. A pharmaceutical composition for use in treating glomerulonephritis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.
- 28. A pharmaceutical composition for use in treating organofibrosis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 1-21.
- 29. A pharmaceutical composition for use in treating leukemia, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable saits according to any one of Claims 1-21.
- 30. A pharmaceutical composition for use in treating articular rheumatism, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically accept-

### EP 0 860 433 A1

able salts according to any one of Claims 1-21.

5

10

1 20

30

55

- 31. A pharmaceutical composition for use in treating glomerulonephritis, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to Claim 5, 8 or 12.
- 32. A pharmaceutical composition for use in treating tumors, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19.
- 33. A pharmaceutical composition for use in treating leukemia, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19.
- 34. A pharmaceutical composition for use in treating articular rheumatism, which comprises at least one compound, as an effective component, selected from the group consisting of the compounds and their pharmaceutically acceptable salts according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19.
  - 35. A method for treating neoplastic tumors, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for neoplastic tumors.
  - 36. A method for treating psoriasis, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for psoriasis.
- 25 37. A method for treating atherosclerosis, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for atherosclerosis.
  - 38. A method for treating restenosis after percutaneous coronary angioplasty or bypass surgery, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for restenosis after percutaneous coronary angioplasty or bypass surgery.
  - 39. A method for treating glomerulonephritis, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for glomerulonephritis.
- 40. A method for treating organofibrosis, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for organofibrosis.
  - 41. A method for treating leukemia, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for leukemia.
  - 42. A method for treating articular rheumatism, which comprises administering an effective amount of the compounds according to any one of Claims 1-21 to patients who need treatment for articular rheumatism.
- 43. A method for treating glomerulonephritis, which comprises administering an effective amount of the compounds according to Claim 5, 8 or 12 to patients who need treatment for glomerulonephritis.
  - 44. A method for treating tumors, which comprises administering an effective amount of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 to patients who need treatment for tumors.
- 45. A method for treating leukemia, which comprises administering an effective amount of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 to patients who need treatment for leukemia.
  - 46. A method for treating articular rheumatism, which comprises administering an effective amount of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 to patients who need treatment for articular rheumatism.
  - 47. Use of the compounds according to any one of Claims 1 to 21 for manufacturing pharmaceutical compositions.

### EP 0 860 433 A1

- 48. Use of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 for manufacturing antitumor agents.
- 49. Use of the compounds according to any one of Claims 7, 10, 11, 14, 15, 16, 17 and 19 for manufacturing therapeutic agents for articular rheumatism.